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| 10/587,841 | 06/18/2008 | Tomoko Nakagawa | 082368-008600US | 6926 |

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| EXAMINER | |
|---|---|
| JUEDES, AMY E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

| NOTIFICATION DATE | DELIVERY MODE |
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| 04/27/2011 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/587,841 | NAKAGAWA ET AL. | |
| | Examiner | Art Unit | |
| | AMY JUEDES | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 February 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-4 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's amendment and remarks, filed 2/24/11, are acknowledged.

Claims 2-3 have been amended.

Claim 22 has been added.

Claims 2-4 and 22 are pending and are under examination.

2. The rejection of the claims under 35 U.S.C. 102 is withdrawn in view of Applicant's amendment to recite an antibody that binds to the extracellular domain of HIDE1.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of antibodies that bind to a protein encoded by a nucleotide sequence that hybridizes to a complementary sequence of an HIDE1 gene under stringent conditions.

As set forth previously, The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

The claims also encompass antibodies that bind to a protein encoded by a nucleic acid sequence that

hybridizes to a HIDE1 gene under stringent conditions. This might encompass antibodies to proteins that comprise a significant number of additions, mutations, or deletions compared to a HIDE1 protein. This might encompass structurally different antibodies that bind to structurally different HIDE1 proteins such as species homologous, splice variants, allelic variants, etc. The specification does not disclose a correlation between the structure of the antibodies and the function of binding to monocytes. Additionally, there is no art recognized correlation between said structure and function. Furthermore, the instant specification only discloses two species of antibody specific for the HIDE1 proteins of SEQ ID NO: 2 and 6 (i.e. human and mouse HIDE1). This is not sufficiently representative of the broad genus of structurally different antibodies encompassed by the instant claims. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

Applicant's arguments filed 2/24/11 have been fully considered, but they are not persuasive.

Applicant argues that the amendment to recite that the HIDE1 proteins are those shown in SEQ ID NO: 2 and 6 obviates the rejection.

The claims encompass antibodies that bind to a protein encoded by a nucleotide sequence that hybridizes to a nucleotide sequence encoding the extracellular domain of HIDE1 as shown in SEQ ID NO: 2 and 6. As noted above, this might encompass antibodies to structurally different proteins with a significant number of additions, mutations, or deletions compared to HIDE1. The specification does not disclose a correlation between the structure of the antibodies and the function of binding to monocytes, and the only species disclosed are antibodies that bind to SEQ ID NO; 2 and 6.

It is noted that new claim 22 is being included in the rejection, since it only specifies that the extracellular domain is amino acids 27 to 117 of SEQ ID NO: 6, but does not require that the antibodies bind to said extracellular domain (i.e. the claims encompass antibodies that bind to a protein encoded by a nucleic acid sequence that hybridizes to a nucleic acid encoding amino acids 27 to 117 of SEQ ID No: 6, for example).

4. Claims 2-4 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for detecting a monocyte or a method for isolating a monocyte

comprising contacting a blood sample with an antibody that binds (a) the extracellular domain of the HIDE1 protein shown in SEQ ID NO: 2 or 6,
does not reasonably provide enablement for:

A method for detecting a monocyte or a method for isolating a monocyte comprising contacting a blood sample with an antibody that binds to (b) a protein encoded by a nucleotide sequence that hybridizes to a complementary sequence of the extracellular domain of the HIDE1 protein shown in SEQ ID NO: 2 or 6.

As set forth previously, The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

With regards to the instant claims, their breadth comprises a primary issue as regards the unpredictability of the claimed method. The instant claims are drawn to a method for detecting/isolating a monocyte comprising contacting a blood cell sample with an antibody that binds to a HIDE1 protein, including a protein encoded by a nucleotide sequence that hybridizes to a HIDE1 gene under stringent conditions. This might encompass using antibodies to structurally different HIDE1 proteins comprising different species homologous, splice variants, allelic variants, or to mutated or variant HIDE1 polypeptides. Additionally, protein chemistry is one of the most unpredictable areas of biotechnology. Whisstock et al (Quarterly Review of Biophysics, 2003, 36, pp307-340) teach that the prediction of protein function from sequence and structure is a difficult problem, because homologous proteins often have different functions. Even single amino acid changes in a proteins amino acid sequence can have dramatic effects on protein function. For example, Wang et al. , 2001, show that a single amino acid determines lysophospholipid specificity of the S1P1 (EDG1) and LPA1 (EDG2) phospholipids growth factor receptors (e.g., abstract). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Thus, it would be highly unpredictable as to whether all the HIDE1 proteins encompassed by the instant claims can act as monocytic markers. Thus, using antibodies to said proteins to isolate or detect monocytes is highly

unpredictable.

Thus given the breadth of the claims and the unpredictability of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The specification discloses that antibodies that specifically bind to the human or mouse HIDE1 shown in SEQ ID NO: 2 or 6 can detect or isolate monocytes. However, no other examples are provided of HIDE1 proteins that can function as monocyte makers. Furthermore, the specification fails to provide any guidance regarding which structural features are required for the polypeptides to function as monocyte markers. Therefore, it would require undue experimentation to isolate or detect monocytes with the antibodies as broadly claimed.

Applicant's arguments filed 2/24/11 have been fully considered, but they are not persuasive.

Applicant argues that the amendment to recite that the HIDE1 proteins are those shown in SEQ ID NO: 2 and 6 obviates the rejection.

The claims encompass antibodies that bind to a protein encoded by a nucleotide sequence that hybridizes to a nucleotide sequence encoding the extracellular domain of HIDE1 as shown in SEQ ID NO: 2 and 6. As noted above, this might encompass antibodies to structurally different proteins with a significant number of additions, mutations, or deletions compared to HIDE1, and protein chemistry is a highly unpredictable art. The specification does not provide any guidance regarding which structural features are required for the polypeptides to function as monocyte markers. Therefore, it would require undue experimentation to isolate or detect monocytes with the antibodies as broadly claimed.

5. The following are new grounds of rejection necessitated by Applicant's amendment.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 4, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/55335 (of record).

WO 01/55335 teaches a method of detecting the protein of SEQ ID NO: 37. SEQ ID NO: 37 of WO 01/55335 is 100% identical to SEQ ID NO: 6 of the instant application. WO 01/55335 teaches a detection method comprising contacting a blood cell sample with an antibody that binds to the protein, and detecting binding of the antibody (see page 7 and 109, in particular). WO 01/55335 teaches antibodies to fragments of the protein of SEQ ID nO:37, and particularly teaches the usefulness of the extracellular fragment of SEQ ID NO: 37 (see pages 17 and 94, in particular). WO 01/55335 also teaches antibodies that bind to the surface of the protein (i.e. the extracellular region, see page 94-95, in particular). WO 01/55335 also teaches detecting SEQ ID NO: 37 is bone marrow (i.e. a sample comprising monocytes, see page 131, in particualr). Thus, the method of WO 01/55335 is identical to that of the instant claims and would inherently detect monocytes.

Thus, the reference clearly anticipates the invention.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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